REMARKS

Claims 1-7 and 10-22 are pending in the present application. Claims 8, 9 and 23-34, have been canceled without prejudice or disclaimer as being drawn to a non-elected invention.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

Restriction Requirement

Page 2 of the Office Action indicates that the restriction requirement has been made final. In view of the finality of the restriction requirement, claims 8, 9 and 23-34, have been cancelled as directed to non-elected subject matter. Applicants hereby reserve the right to pursue the subject matter of the cancelled claims in one or more divisional patent applications.

Claim Rejections Under 35 U.S.C. § 103.

Claims 1-7 and 10-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rossi *et al.*, (*Hybridoma*, 11(3):333-338, 1992) in view of May (GB 2,204,398).

Applicants respectfully disagree and traverse the rejection. Applicants' invention recites in claim 1, a lateral flow immunoassay device for identifying the presence of tissue from a particular species of billfish in a test sample The device comprises a substrate onto which a billfish specific antigen-containing sample has been immobilized. The substrate is preferably a plastic backed porous nitrocellulose membrane, see for example, page 6, lines 1-9. The device can be partially enveloped with a rigid cover with at least one aperture for applying a test sample and can optionally include a transparent window for detecting color development.

Furthermore, the instant invention discloses a lateral flow immunoassay device that is configured for both a **direct and an indirect** immunoassay. (See for example, page 6, lines 10-11). The indirect immunoassay is simple, inexpensive and fast as disclosed on page 2, lines 13-23:

> In one aspect, this invention particularly relates to a lateral flow competitive immunoassay that utilizes a colloidal gold-monoclonal antibody probe for the qualitative detection of billfish serum albumin. The latter assay involves mixing a fish sample with a colloidal gold-monoclonal antibody conjugate and applying the mixture to one end of a plastic-backed nitrocellulose membrane strip with a filter paper slip at the opposite end as a wick. The presence of albumin in a target sample competes with adsorbed antigen to prevent the appearance of a pink color on the nitrocellulose membrane. A non-target sample yields a pink color when colloidal gold-labeled monoclonal antibodies bind to billfish albumin previously absorbed to the nitrocellulose. The assay requires only five minutes to perform and utilizes two inexpensive solutions.

The detection of billfish specific antigens can be also based on a **negative** result. (See above).

Rossi is an irrelevant prior art reference as it fails to teach or suggest a **lateral flow immunoassay** device. Rossi discloses an **indirect enzyme-linked plate assay**. The Examiner has acknowledged that Rossi is **not prior art**. See Office Action, on page 2, last paragraph:

> Rossi differs from the instant invention in failing to teach a lateral flow device using nitrocellulose and various reagents that are conventional in a lateral flow assay device such as gold sol label.

In contrast to the instant invention, May discloses a **two zone** detection assay. The two zones are "spatially distinct," see for example May, page 3, lines 28-31, and **require two antibodies**. The first antibody is a labeled antibody which is immobilized in the first zone. The second zone requires use of a second unlabeled antibody which is

"permanently immobilized." (See, for example, page 3, line 13). Therefore, May discloses the use of **two** different antibodies in **two** zones. The first antibody is allegedly mobile when a moist sample is added and the second antibody is allegedly permanently immobilized. Each antibody is directed to different epitopes. May's disclosure, therefore, requires **the use of pre-prepared devices** that **can only detect antigens for a pre-determined test**. That is, in a field condition, devices which have been prepared, for example, pregnancy, could only be used to detect hormones for which the device has been prepared. The device does not provide for flexibility in that **each device** must **contain the appropriate antibodies for the appropriate test**. Also, unanticipated field moist conditions prior to addition of a sample would thus reduce the ability of May's device to detect a desired antigen as the first antibody would diffuse through the device, prior to the addition of a moist sample.

In contrast, claim 1 recites a lateral flow device having a billfish specific antigen-containing sample immobilized on a substrate. The sample can be, for example, "whole blood, serum or tissue homogenates." (See, for example, page 2 lines 11-13). In addition, applicants invention differs from May in that applicants disclose the **immobilization of a test sample**. That is, **any** sample can be immobilized requiring the addition of **one** desired antibody for detection. Thus, applicants' device is ready for use **under any conditions for any sample** and **is not limited** in specificity by devices already containing immobilized antibodies wherein the device is useful for only for pre-designated tests as disclosed by May.

The Office Action states on page 3, first paragraph, "May teaches the use of direct labels such as minute colored particles, such as dye sols, metallic soles and colored latex particles." However, as discussed *supra*, these antibodies "become mobile" when in a moist state **and** require a second permanently immobilized antibody to detect antigen. May, therefore, teaches away from using a device wherein the **sample is immobilized** and a billfish specific antibody is added for detection of antigen. One of ordinary skill in

the art is aware that different conditions (e.g. type of solution, pH, salt, etc) affect both the conformation and binding abilities of antibody including the stability of the bond between the antibody and the label. Especially so, since a lateral flow antibody based assay for detecting proteins from fish species caught in the wild would require coupling gold particles to either the antibody or the fish albumin and determining if conjugation affects their ability to interact. May does not disclose or suggest how any of the antibodies would be suitable for use in a lateral flow immunoassay device.

Furthermore, undue experimentation would be required to determine the suitability of producing antibodies that would detect billfish specific antigen. For example, May does not teach or suggest production of antibodies that are : (1) in a form which allows them to become mobile in moist conditions without changing the specificity or avidity of the antibody; (2) a second antibody that is permanently immobilized and can still recognize an antigen already bound to a detectably labeled-antibody (e.g. a gold conjugated antibody); and, (3) differentiate between closely related species. May does not teach or suggest which epitopes these antibodies would have to be directed to and how any of these or other conditions would affect antibody-antigen recognition. It is well-known to one of ordinary skill in the art that antibodies recognize conformational epitopes and the device taught by May would simply not work when applied to the instant application. Other problems include whether any of the antigens coupled with the antibodies **would even migrate to the second zone.** For example, the antigen-antibody complex of the first zone may be too large to diffuse to the second zone, thus, decreasing any possibility of detection by May's device.

In view of the combination of the failure of Rossi *et al.* as a prior art reference and failure to teach or suggest the use of a lateral flow gold conjugate device with the failure of the May reference to teach or suggest detection of billfish specific antigens as disclosed by the instant invention, Applicants submit that one of ordinary skill in the art

would have no motivation to combine the references in the manner suggested in the instant Office Action.

Indeed such motivation can only be provided by an application of the teachings of the instant invention, and such is improper as it constitutes a hindsight reconstruction of Applicants' invention.

Therefore, Applicants submit that claims 1-7 and 10-22, are patentable over Rossi *et al.* in view of May *et al.*

Applicants would also like to point out other patentable embodiments of the application. For example, claim 13 is directed to detection of a billfish specific antigen in the lateral flow immunoassay device based on a **gold**-conjugated monoclonal antibody. The novelty and importance of the instant invention is that the gold-conjugated monoclonal antibody detects bill-fish specific antigens among **closely-related species** of fish. (See for example, page 8, lines 19-20).

Rossi *et al.* in view of May *et al.* are silent regarding the use of gold-conjugated antibodies that are specific for billfish antigens in a lateral flow immunoassay device.

CONCLUSION

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1-7 and 10-22 is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned directly at (561) 653-3662 between the hours of 9 a.m. to 7 p.m., Monday - Friday.

In re: Application of: HARTMANN et al.
Application No.: 09/990,718
Examiner: Nguyen, B. T. L.

Respectfully submitted,

Dated: 5/19/14

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